Common Sexually Transmitted Diseases: STD 101 for Clinicians

Something for Everyone!

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for STD101
Topics

• Background Information
• “Sores”
• “Drips”
Background Information
## Burden of STD in U.S.

<table>
<thead>
<tr>
<th>STD</th>
<th>Cases Reported</th>
<th>Rate (per 100K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td>1.3 million (2010)</td>
<td>426</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>309,341 (2010)</td>
<td>100.8</td>
</tr>
<tr>
<td>Syphilis (P &amp; S)</td>
<td>13,774 (2010)</td>
<td>4.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>STD</th>
<th>Estimated New Cases</th>
<th>Prevalent Cases/%</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV</td>
<td>1.6 million (2000)</td>
<td>16.2% (2005-8)</td>
</tr>
<tr>
<td>HPV</td>
<td>6.2 million (2000)</td>
<td>26.8% F (2003-4)/</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.3-72.9% M</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>7.4 million (2000)</td>
<td>2.3 million (2001-4)</td>
</tr>
<tr>
<td>HIV</td>
<td>48,100 (2009)</td>
<td>&gt;600,000 (2008)</td>
</tr>
</tbody>
</table>

Background

STIs Facilitate HIV Transmission

- Disruption of epithelial/mucosal barriers
- Increase the number of HIV target cells in the genital tract
- Increase expression of HIV co-receptors
- Induce secretion of cytokines (increase HIV shedding)
- HIV alters natural history of some STIs

Fleming DT and Wasserheit JN. From Epidemiological Synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sex Transm Inf* 1999;75:3-17.

Slide courtesy of AL/NC STD/HIV Prevention Training Center
Where Do People Go for STD Treatment?

- Population-based estimates from National Health and Social Life Survey

<table>
<thead>
<tr>
<th>Location</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Private provider</td>
<td>59%</td>
</tr>
<tr>
<td>Other clinic</td>
<td>15%</td>
</tr>
<tr>
<td>Emergency room</td>
<td>10%</td>
</tr>
<tr>
<td>STD clinic</td>
<td>9%</td>
</tr>
<tr>
<td>Family planning clinic</td>
<td>7%</td>
</tr>
</tbody>
</table>

Chlamydia—Percentage of Reported Cases by Sex and Selected Reporting Sources, United States, 2010

*HMO = health maintenance organization; HD = health department.

NOTE: These categories represent 72.5% of cases with a known reporting source. Of all cases, 11.6% had a missing or unknown reporting source.
Percent* of Women Who Said Topic Was Discussed During First Visit With New Gynecological or Obstetrical Doctor/Health Care Professional

<table>
<thead>
<tr>
<th>Topic</th>
<th>HCP asked</th>
<th>Pt. asked</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Self Exam</td>
<td>69%</td>
<td>4%</td>
</tr>
<tr>
<td>Pap Smear</td>
<td>60%</td>
<td>12%</td>
</tr>
<tr>
<td>Birth Control</td>
<td>33%</td>
<td>20%</td>
</tr>
<tr>
<td>Mammograms</td>
<td>34%</td>
<td>7%</td>
</tr>
<tr>
<td>Sexual History and/or Current...</td>
<td>36%</td>
<td>3%</td>
</tr>
<tr>
<td>Alcohol Use</td>
<td>24%</td>
<td>1%</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>19%</td>
<td>2%</td>
</tr>
<tr>
<td>STDs other than HIV/AIDS</td>
<td>12%</td>
<td>3%</td>
</tr>
</tbody>
</table>

*Percentages may not total to 100% because of rounding or respondents answering “Don’t know” to the question “Who initiated this conversation?”

Source: Kaiser Family Foundation/Glamour National Survey on STDs, 1997
“...the scope and impact of the STD epidemic are under-appreciated and the STD epidemic is largely hidden from public discourse.”

IOM Report 1997
STDs of Concern

• “Sores” (ulcers)
  – Syphilis
  – Genital herpes (HSV-2, HSV-1)
  – Others uncommon in the U.S.
    • Lymphogranuloma venereum
    • Chancroid
    • Granuloma inguinale
STDs of Concern (continued)

• “Drips” (discharges)
  – Gonorrhea
  – Chlamydia
  – Nongonococcal urethritis / mucopurulent cervicitis
  – Trichomonas vaginitis / urethritis
  – Candidiasis
  – Bacterial vaginosis

• Other major concerns
  – Genital HPV (especially type 16, 18) and Cervical/Anal/Oral Cancer
“Sores”

Syphilis

Genital Herpes (HSV-2, HSV-1)
Genital Ulcer Diseases – Does It Hurt?

• Painful
  – Chancroid
  – Genital herpes simplex

• Painless
  – Syphilis
  – Lymphogranuloma venereum
  – Granuloma inguinale
Primary Syphilis – Clinical Manifestations

• Incubation: 10-90 days (average 3 weeks)

• Chancre
  – Early: macule/papule → erodes
  – Late: clean based, painless, indurated ulcer with smooth firm borders
  – Unnoticed in 15-30% of patients
  – Resolves in 1-5 weeks
  – HIGHLY INFECTIOUS
Primary Syphilis Chancre

Source: Florida STD/HIV Prevention Training Center
Primary Syphilis

Source: Centers for Disease Control and Prevention
Secondary Syphilis - Clinical Manifestations

- Represents hematogenous dissemination of spirochetes
- Usually 2-8 weeks after chancre appears
- Findings:
  - rash - whole body (includes palms/soles)
  - mucous patches
  - condylomata lata - HIGHLY INFECTIOUS
  - constitutional symptoms
- Sn/Sx resolve in 2-10 weeks
Secondary Syphilis Rash

Source: Florida STD/HIV Prevention Training Center
Secondary Syphilis: Generalized Body Rash

Source: CDC/NCHSTP/Division of STD Prevention, STD Clinical Slides
Secondary Syphilis Rash

Source: Florida STD/HIV Prevention Training Center
Secondary Syphilis Rash

Source: Cincinnati STD/HIV Prevention Training Center
Secondary Syphilis

Source: Diepgen TL, Yihune G et al. Dermatology Online Atlas
Secondary Syphilis – Condylomata Lata

Source: Florida STD/HIV Prevention Training Center
Early Syphilis – Diagnosis and Treatment

- **Diagnosis:**
  - Clinical presentation
  - Darkfield
  - Serology

- **Treatment:**
  - Benzathine PCN G 2.4 million units x 1
Genital Herpes Simplex - Clinical Manifestations

- Transmission through direct contact – may be with asymptomatic shedding
- Primary infection commonly asymptomatic; symptomatic cases sometimes severe, prolonged, systemic manifestations
- Vesicles $\Rightarrow$ painful ulcerations $\Rightarrow$ crusting
- Recurrence a potential
## HSV-2 Infection: Who knows it?

<table>
<thead>
<tr>
<th></th>
<th>% Seropositive for HSV-2</th>
<th>% Reporting history of genital herpes</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHANES III</td>
<td>21.9</td>
<td>2.6</td>
<td>9.2</td>
</tr>
<tr>
<td>Black</td>
<td>21.9</td>
<td>2.6</td>
<td>9.2</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2.6</td>
<td>3.7</td>
<td>3.7</td>
</tr>
<tr>
<td>White</td>
<td>9.2</td>
<td>3.8</td>
<td>3.8</td>
</tr>
<tr>
<td>Suburban MD Office</td>
<td>25.5</td>
<td>4.3</td>
<td>11.9</td>
</tr>
<tr>
<td>Project Respect</td>
<td>41</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>JCDH STD-males</td>
<td>45</td>
<td>6</td>
<td>36 (3 questions)</td>
</tr>
</tbody>
</table>

HSV: Diagnosis and Treatment

- **Diagnosis:**
  - Culture
  - Serology (Western blot)
  - PCR

- **Treatment:**
  - Acyclovir
  - Valacyclovir
  - Famciclovir
Genital Herpes Simplex

Source: Diepgen TL, Yihune G et al. Dermatology Online Atlas
Genital Herpes Simplex

Source: CDC/NCHSTP/Division of STD, STD Clinical Slides
Genital Herpes Simplex in Females

Source: Centers for Disease Control and Prevention
Genital Herpes Simplex

Source: Florida STD/HIV Prevention Training Center
“Drips”

Gonorrhea
Nongonococcal urethritis
Chlamydia
Mucopurulent cervicitis
Trichomonas vaginitis and urethritis
Bacterial vaginosis
Gonorrhea - Clinical Manifestations

- **Urethritis - male**
  - Incubation: 1-14 d (usually 2-5 d)
  - Sx: Dysuria and urethral discharge (5% asymptomatic)
  - Complications

- **Urogenital infection - female**
  - Endocervical canal primary site
  - 70-90% also colonize urethra
  - Incubation: unclear; sx usually in 10 d
  - Sx: majority asymptomatic; may have vaginal discharge, dysuria, urination, labial pain/swelling, abdominal pain
  - Complications
Gonorrhea

Source: Florida STD/HIV Prevention Training Center
Gonorrhea Gram Stain

Source: Cincinnati STD/HIV Prevention Training Center
Nongonococcal Urethritis

Source: Diepgen TL, Yihune G et al. Dermatology Online Atlas
Nongonococcal Urethritis

• **Etiology:**
  – 20-40% *C. trachomatis*
  – 20-30% genital mycoplasmas (*Ureaplasma urealyticum, Mycoplasma genitalium*)
  – Occasional *Trichomonas vaginalis, HSV*
  – Unknown in ~50% cases

• **Sx:** Mild dysuria, mucoid discharge

• **Dx:** Urethral smear $\geq$ 5 PMNs (usually $\geq$15)/OI field
  Urine microscopic $\geq$ 10 PMNs/HPF
  Leukocyte esterase (+)
Mucopurulent Cervicitis

Source: Seattle STD/HIV Prevention Training Center
Chlamydia Life Cycle

Source: California STD/HIV Prevention Training Center
**Chlamydia trachomatis**

- **Clinical Manifestations:**
  - Mostly asymptomatic
  - cervicitis, urethritis, proctitis, lymphogranuloma venereum, and pelvic inflammatory disease

- **Complications:** Potential to transmit to newborn during delivery
  - Conjunctivitis, pneumonia
Normal Cervix

Source: Claire E. Stevens, Seattle STD/HIV Prevention Training Center
Chlamydia Cervicitis

Source: St. Louis STD/HIV Prevention Training Center
Laboratory Testing: CT and GC

- Gram stain (gonorrhea)
- Culture
- Non-culture non-amplified tests
- Commercially available NAATs include:
  - Becton Dickinson *BDProbeTec*®
  - Gen-Probe *AmpCT, Aptima*®
  - Roche *AmpliCor*®
- Specimen types: urine, cervical, urethral, vaginal, liquid PAP (not as sensitive)
- Serology (CT in setting of LGV)
2010 CDC STD Treatment Guidelines: Gonorrhea

• Recommended
  – Ceftriaxone 250 mg IM x 1
    OR IF NOT AN OPTION...
  – Cefixime 400 mg PO x 1 Or
  – Single-dose injectible cephalosporin regimens
    PLUS
  – Azithromycin 1gm PO x 1 Or
  – Doxycycline 100mg PO BID x 7d
2010 CDC STD Treatment Guidelines
Chlamydia/NGU

Recommended:
Azithromycin 1gm po x 1 Or
Doxycycline 100mg po BID x 7d

Alternative:
Erythromycin base 500mg po QID x 7d Or
Erythromycin EES 800mg po QID x 7d Or
Levofloxacin 500mg po qd x 7d Or
Ofloxacin 300mg po BID x 7d
Pelvic Inflammatory Disease (PID)

• 10%-20% women with GC develop PID
• In Europe and North America, higher proportion of *C. trachomatis* than *N. gonorrhoeae* in women with symptoms of PID
• CDC minimal criteria
  – uterine adnexal tenderness, cervical motion tenderness
• Other symptoms include
  – endocervical discharge, fever, lower abdominal pain
• Complications:
  – Infertility: 15%-24% with 1 episode PID secondary to gonorrhea or chlamydia
  – 7X risk of ectopic pregnancy with 1 episode PID
  – chronic pelvic pain in 18%
Pelvic Inflammatory Disease

Source: Cincinnati STD/HIV Prevention Training Center
C. trachomatis Infection (PID)

Normal Human Fallopian Tube Tissue

PID Infection

Source: Patton, D.L. University of Washington, Seattle, Washington
2010 CDC STD Treatment Guidelines: PID Outpatient Treatment

- Ceftriaxone 250mg IM x 1 PLUS doxycycline 100mg po BID x 14d +/- metronidazole 500mg po BID x 14d
- Cefoxitin 2g IM x 1 and probenecid 1g po x 1 PLUS doxycycline 100mg po BID x 14d +/- metronidazole 500mg po BID x 14d
- Other parenteral third generation cephalosporin PLUS doxycycline 100mg po BID x 14d +/- metronidazole 500mg po BID x 14d
Trichomonas vaginalis

- Sexually transmitted parasite
- Most common treatable STD
- Estimated prevalence:
  - 7.9-13% in the general female population
    - Prevalence increases with age
    - Highest rates in AA (20.2%)
    - Highest rates in southeast (14.4%)
  - 6.1% to 33% prevalence in HIV+ women using wet prep +/- culture; up to 52.6% with nucleic acid amplification testing
- Several studies support the epidemiological association between TV and HIV and decreased genital HIV shedding with treatment of TV

Clinical Manifestations of

*T. vaginalis*

MOST TRICHIOMONAL INFECTIONS ARE ASYMPTOMATIC!!!
Diagnostic Tests for TV

• **Females**
  - Wet prep
  - Culture
  - OSOM Trichomonas Rapid Test (Genzyme Diagnostics, Cambridge, Massachusetts)
  - Affirm™ VP III (Becton Dickenson, San Jose, California) *T. vaginalis, G. vaginalis*, and *C. albicans*.
  - Gen-Probe APTIMA Combo 2®

• **Males**
  - Culture (multiple specimen types)
  - Gen-Probe APTIMA Combo 2®
  - Roche COBAS® Amplicor PCR
2010 CDC STD Treatment Guidelines: *Trichomonas vaginalis*

**Recommended:**
- Metronidazole 2gm PO x 1 dose Or
- Tinidazole 2gm PO x 1 dose

**Alternative:**
- Metronidazole 500mg PO BID x 7d*

*Consider as preferred in HIV-infected women*
Bacterial Vaginosis

- Polymicrobial clinical syndrome characterized by loss of H$_2$O$_2$-producing lactobacillus sp.
- Most common cause of vaginitis/osis
- Prevalence varies by population:
  - 5%-25% among college students; 12%-61% among STD patients
- Complications:
  - Premature rupture of membranes, premature delivery, low birth-weight delivery, acquisition of HIV, development of PID, post-operative infections after gynecological procedures
Bacterial Vaginosis

• 50% asymptomatic
• Signs/symptoms when present:
  – malodorous (fishy smelling) vaginal discharge
• Diagnosis:
  – Amsel Criteria, vaginal Gram stain, rapid tests
Indication to treat BV:

Symptoms!
**Bacterial Vaginosis Treatment**

**CDC-recommended regimens:**
- Metronidazole 500 mg orally twice a day for 7 days
- Metronidazole gel 0.75%, one full applicator (5 grams) intravaginally, once a day for 5 days
- Clindamycin cream 2%, one full applicator (5 grams) intravaginally at bedtime for 7 days

**Alternative regimens:**
- Tinidazole 2gm po qd x 2 days
- Tinidazole 1gm po qd x 5 days
- Clindamycin 300 mg orally twice a day for 7 days
- Clindamycin ovules 100 g intravaginally once at bedtime for 3 days
HPV: Epidemiology

• Among sexually active women*: 
  – >50% have been infected with one or more genital types
  – 15% have current infection
    • 50-75% of these are high-risk
    • 1% have genital warts
• Prospective study of young women#
  – 36mo incidence rate of 43%
• NHANES survey – 26.8% women 14-59 with detectable HPV DNA (vaginal swabs)

#Ho et al. NEJM. 1998
HPV

• Transmission: skin-to-skin contact

• High-risk (16, 18 etc) vs low-risk (6, 11 etc) types
  – Low-risk types: genital warts
  – High-risk HPV infection is causally associated with cervical cancer and other anogenital squamous cell cancers (e.g. anal, penile, vulvar, vaginal)

• Diagnosis: Clinical exam, cytology, nucleic acid amplification methods (in conjunction with cytology for high-risk HPV types)

• Treatment: Topical and destructive modalities
HPV-Associated Cervical Cancer

- 400,000-500,000 cases of cervical cancer per year world-wide
- In US, rates down but still 12,280 cases and 4,021 deaths from cervical cancer in 2007

Anal SCCA

- Incidence of squamous cell cancer of the anus (SCCA) in the United States has increased by ~96% in men and ~39% in women
- Incidence of anal cancer in MSM estimated to be 35 cases / 100,000 population
  - This is comparable to the incidence of cervical cancer before the introduction of routine pap screening

Perianal Warts

Source: Cincinnati STD/HIV Prevention Training Center
HPV Penile Warts

Source: Cincinnati STD/HIV Prevention Training Center
Intrameatal Wart of the Penis (and Gonorrhea)

Source: Florida STD/HIV Prevention Training Center
HPV Cervical Warts

Source: Cincinnati STD/HIV Prevention Training Center
HPV Warts on the Thigh

Source: Cincinnati STD/HIV Prevention Training Center
Possible HPV on the Tongue

Source: Cincinnati STD/HIV Prevention Training Center
HPV Vaccines - Females

Cervarix™ – GSK
• HPV 16 and 18
• 0, 1, 6mo dosing
• Females 10-25yrs
• Approved 10/09

Gardasil™ - Merck
• HPV types 6,11,16,18
• 0, 2, 6mo dosing
• Females 9-26yrs
• Approved 6/06

Efficacy approximately 100% against precancerous lesions caused by specific types in the vaccine!
Gardasil for Males

• Initial study demonstrated 90% efficacy for preventing external lesions caused by HPV types 6, 11, 16 and 18 in men 16-26y

• FDA approved (10/09) for males 9-26 for prevention of genital warts
Gardasil for Anal Cancer Prevention

- HPV associated with approximately 90% of anal cancer
- Vaccine approved for new indication December 22, 2010
- Males and females 9-26 years of age
- Prevention of anal cancer and associated precancerous lesions caused by HPV types 6, 11, 16, 18
Questions?